

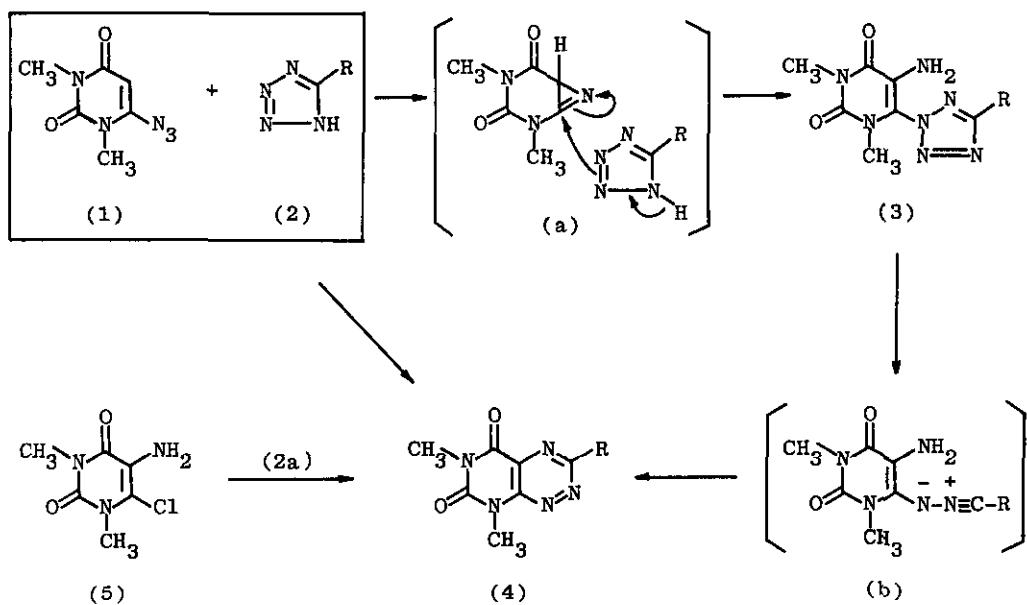
A NEW SYNTHESIS OF FERVENULINS AND ALLOXAZINES. THERMOLYSIS
AND PHOTOLYSIS OF 6-AZIDO-1,3-DIMETHYLURACIL WITH TETRAZOLES
AND BENZOTRIAZOLES

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Abstract — Thermolysis of 6-azido-1,3-dimethyluracil(1) in the presence of 5-substituted tetrazoles(2) gave 3-substituted fervenulins(4), which were also synthesized from the intermediates(3) prepared by photolysis of (1) with (2). Irradiation of (1) with benzotriazoles(6) in tetrahydrofuran gave 6-(benzotriazol-1-yl)uracils(7), which were irradiated in methanol to afford alloxazines(8).

Azido compounds display a variety of thermochemical and photochemical reactivities via a nitrene intermediate¹⁾. We have recently reported²⁾ the photochemical reaction of 6-azido-1,3-dimethyluracil (1) in the presence of nucleophiles and their application to the facile synthesis of lumazines and fervenulins. Meanwhile, tetrazoles and benzotriazoles as well as azides lose nitrogen on thermolysis or photolysis to give unstable intermediates such as nitrilimine, carbene, and bi-radical³⁾. During our investigation of thermolysis and photolysis of (1) with tetrazoles or benzotriazoles, we have found a new procedure for the synthesis of fervenulins and alloxazines.

Treatment of (1) with an equivalent of 5-phenyltetrazole(2a) in refluxing dimethylformamide(DMF) for 30 minutes afforded 3-phenylfervenulin(4a), in 75% yield, which was identical with an authentic sample²⁾. When a solution of (1) and (2a) in tetrahydrofuran(THF) was irradiated with a 100 W high-pressure mercury lamp through a Pyrex filter for 3 hours, 5-amino-1,3-dimethyl-6-(5-phenyltetrazol-2-yl)uracil(3a)⁴⁾ was obtained in 70% yield. Further irradiation of (3a) in THF recovered it unchanged but in methanol afforded (4a) in 85% yield. The fervenulin (4a) was also synthesized by refluxing of (3a) in DMF or by treatment of 5-amino-



Scheme I

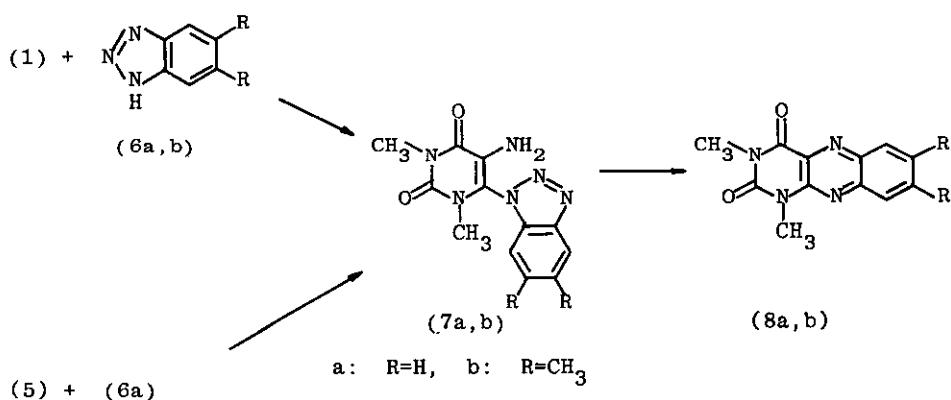
Table Formation of 5-Amino-6-(tetrazol-2-yl)uracils(3) and Fervenulins(4)

R	(3a) - (3e)		(4a) - (4e)			
	m.p.(dec.) °C	Yield %	m.p. °C	Yield %		
				from (1)	from (3)	
				hν	Δ	
a C_6H_5	143-144	70	278-279	70	85	90
b $3-\text{CH}_3\text{C}_6\text{H}_4$	150-153	70	286-288	80	78	82
c $4-\text{CH}_3\text{C}_6\text{H}_4$	135-137	71	273-275	85	73	80
d $\text{C}_6\text{H}_5\text{CH}_2$	198	65	190-192	60	78	80
e CH_3S	148-150	63	157-160	40	85	85

6-chloro-1,3-dimethyluracil(5) with (2a) in the presence of potassium carbonate in DMF at 130°. These results suggest that compound (3a) is an intermediate in the thermolysis of (1a) with (2a) into (4a). Respective mechanisms for the formation of (3) and (4) would involve a nucleophilic attack by the tetrazole on an azirine intermediate (a) and a cyclization of a nitrilimine intermediate (b) as described previously^{2,5}.

Other 3-substituted fervenulins (4b-4e) and intermediates (3b-3e) were similarly prepared as summarized in Table⁶.

Similar reactions of benzotriazole (6a) with (1) did not occur under the same thermo- and photo-chemical conditions. However, the photolysis in the presence of triethylamine in THF proceeded smoothly with the formation of the 6-(benzotriazol-1-yl)uracil intermediate (7a)(mp 238°, 70%), whose structure was confirmed by comparison of authentic (7a) prepared by treatment of (5) with (6a) in refluxing DMF. Compound (7a) was re-irradiated in methanol to be cyclized to 1,3-dimethylalloxazine (8a)⁷(mp 244°, 82%) with loss of nitrogen. 1,3,7,8-tetra-methylalloxazine (8b)⁸ was similarly prepared in 81% yield via the intermediate (7b)(mp 230-232°, 61%).



Scheme II

REFERENCES AND NOTES

- 1) For a review, see "The Chemistry of Azido Group", S. Patai Ed., Interscience, New York, N. Y., 1971.
- 2) S. Senda, K. Hirota, T. Asao, and K. Maruhashi, J. Amer. Chem. Soc., 100, 7661 (1978).
- 3) R. M. Kellogg "Photochemistry of Heterocyclic Compounds", O. Buchardt Ed., Wiley-Interscience, New York, N. Y., 1976, pp 403-413; R. N. Butler, Advances in Heterocyclic Chemistry, 21, 323(1977).
- 4) Typical spectroscopic data for (3a) were : $^1\text{H-n.m.r. (DMSO-d}_6^6)$ δ 2.84 (s, NCH_3), 3.30 (s, NCH_3), 5.05 (brs, NH_2 , deuterium exchangeable); i.r. (KBr disk) 3300 and 3430 cm^{-1} (NH_2); u.v. λ_{max} (EtOH) 242 nm (sh, $\epsilon=1.72\times 10^4$), 275 (1.22×10^4). Data for (3b) - (3e) were analogous.
- 5) For analogous photo- and thermo-elimination of nitrogen from 2,5-disubstituted tetrazoles, see J. S. Clovis, A. Eckell, R. Huisgen, and R. Sustmann, Chem. Ber., 100, 60(1967).
- 6) All new compounds described here gave satisfactory elemental analyses and spectral data.
- 7) H. Goldner, G. Dietz, and E. Carstens, Ann., 694, 142(1966).
- 8) P. Hemmerich, B. Prijs, and H. Erlenmeyer, Helv. Chim. Acta, 43, 372(1960).

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